

ABSTRACT

Molecular Biology

OTX2 ENHANCES GNRH GENE EXPRESSION. Amanda L. Pearson¹, Andrew Wolfe², Sally Radovick², and Helen H. Kim^{*1,2}, University of Chicago, Department of Obstetrics and Gynecology¹, and the Section of Endocrinology², Chicago, Illinois 60637, rovina@uchicago.edu

Gonadotropin-releasing hormone (GnRH) is the primary regulator of reproduction. GnRH is synthesized and released by GnRH neurons in the hypothalamus and acts on pituitary gonadotrophs to regulate the production of gonadal steroids. Two binding sites for the Otx2 homeodomain protein have been found in a 107 bp region essential for neuron-specific expression of the mouse GnRH (mGnRH) gene. Otx2 is a transcription factor important for normal brain development. Here, we detected Otx2 messenger RNA (mRNA) in the mouse hypothalamus, as well as in the GT1-7 line of immortalized GnRH-secreting neurons. Transient transfection studies in GT1-7 cells suggested that mutations to the Otx2 binding sites that inhibit binding decrease mGnRH promoter activity. Over-expression of Otx2 in Gn11 cells, another GnRH-secreting neuronal cell line, lead to an increase in mGnRH promoter activity. Also, knock-down of endogenous Otx2 using RNAi in GT1-7 cells appeared to decrease mGnRH promoter activity. Our findings indicate that Otx2 may play a critical role in the neuronal expression of the mouse GnRH gene.